

## **REMARKS**

Claims 1, 3-14, 44, and 59-70 are pending in this application for the Examiner's review and consideration. Independent claim 1 was amended to delete the recitation that the composition can be an orally administered composition. Claim 1, as amended, recites that the composition is an injectable composition. Accordingly, dependent claim 2, directed to an injectable composition was canceled. Independent claim 44 was also amended to recite that the composition is an injectable composition, *i.e.* to include the limitation of claim 58. Accordingly, claim 58 was canceled and claims 59-60, 62-63, 65, 67, and 69-70, which depended from claim 58, were amended to depend from claim 44. Claims 45-57, directed to compositions for oral administration, were also canceled. Claims 15-43 were previously canceled in response to a Restriction Requirement. Independent claims 1 and 44 were also amended to more clearly recite that the salt is "a salt formed of the pharmacologically active compound and a lipophilic counterion" (Specification at ¶ [0033]). Applicant reserves the right to pursue the canceled claims and other unclaimed subject matter in one or more continuation applications. No new matter is added by these claim amendments so that their entry at this time is warranted.

Applicants appreciate the courtesies extended to Applicants' attorney, Paul E. Dietze, in a telephonic interview on April 1, 2008. The remarks provided below are in substantial accordance with and follow up on the discussions held during the interview. Accordingly, this Amendment is being submitted to satisfy the requirements of 37 CFR §1.133(b).

### **THE REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH)**

The Examiner asserted in the Office Action that "[c]laims 2-14, 45-54, and 56-57 are rejected as being indefinite to the extent that they read on the rejected base claim." It was unclear what was meant by this rejection because it was included as part of a rejection under 35 U.S.C. § 103(a). The Examiner, however, clarified in the Advisory Action that the beginning of the paragraph was inadvertently cut off and indicated that the rejection was a rejection under 35 U.S.C. § 112, second paragraph, that the term "over time" was indefinite, as set forth in the May 4, 2007 Office Action.

Specifically, the Examiner asserted that the phrase "over time" in claim 1 is indefinite

because “it is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention” (May 4, 2007 Office Action, page 5). Applicants respectfully traverse. As discussed in the interview, the specification clearly defines what is meant by the phrase “over time.” The specification clearly recites

By releasing the pharmacologically active compound “over time” is meant that the active compound is present in the blood or treated tissue of the mammal at pharmaceutically effective amounts for at least 2 days after administration.

(See, Specification, ¶ [0016]). The specification also clearly defines the term “pharmaceutically effective amount” (*Id.* at ¶ [0016]). Accordingly, Applicants respectfully submits that the specification does “provide a standard for ascertaining the requisite degree” and, therefore, that the phrase “over time” in claim 1 is not indefinite. Indeed, during the interview the Examiner agreed that, in view of the disclosure in the specification at ¶ [0016], the phrase “over time” in claim 1 is not indefinite.

For the reasons set forth above, Applicants respectfully request that the rejection of claims 1-14 and 45-57 under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

#### **THE REJECTIONS UNDER 35 U.S.C. § 103(A)**

##### **The Rejection of Claim 1 as Being Obvious Over U.S. Patent No. 5,719,197 to Kanios *et al.***

Claim 1 was rejected under 35 U.S.C. § 103(a) as being obvious over U.S. patent no. 5,719,197 to Kanios *et al.* (“Kanios”) for the reasons set forth on pages 2-3 of the Office Action. As discussed above, independent claim 1, as amended, includes the limitation of canceled dependent claim 2, *i.e.*, that the composition is an injectable composition. Claim 2, directed to an injectable composition, was not rejected over Kanios. Accordingly, the rejection of claim 1, as amended, is rendered moot.

##### **The Rejection of Claims 1, 44, 45-48, 50, 51, 54, and 55-13 Under 35 U.S.C. § 103(a) as Being Obvious Over U.S. Patent No. 7,011,846 to Shojaei *et al.***

Claims 1, 44, 45-48, 50, 51, 54, and 55 were rejected under 35 U.S.C. § 103(a) as being

obvious over U.S. patent no. 7,011,846 (“Shojaei”) for the reasons set forth on pages 3-4 of the Office Action. As discussed above, independent claims 1 and 44, as amended, include the limitation of canceled dependent claims 2 and 58, respectively, *i.e.*, that the compositions are injectable compositions. Claims 2 and 58, directed to injectable compositions, were not rejected over Shojaei. Accordingly, the rejection of claims 1, 44, 45-48, 50, 51, 54, and 55, as amended, is rendered moot.

**The Rejection of Claims 1-5, 11, 12, 44, 45-48, 50, 51, 54, 55, 58-61, 67, and 68 Under 35 U.S.C. § 103(a) as Being Obvious Over U.S. Patent No. 6,174,540 to Williams *et al.***

Claims 1-5, 11, 12, 44, 45-48, 50, 51, 54, 55, 58-61, 67, and 68 were rejected under 35 U.S.C. § 103(a) as being obvious over U.S. patent no. 6,174,540 (“Williams”) for the reasons set forth on pages 4-5 of the Office Action. Specifically, the Examiner alleges that Williams teaches an injectable formulation comprising an active agent, such as an antibiotic, and a water immiscible solvent, hydrogenated castor oil, and capric acid. Applicants respectfully traverse.

As the Examiner is aware, in order to render claims obvious under 35 U.S.C. § 103(a), the prior art must disclose or suggest every limitation of the claimed invention and provide the person of skill in the art with a reasonable expectation that the invention will work for its intended purpose. *KSR International Co. v. Teleflex Inc. et al.*, 127 S. Ct. 1727 at 1739-41 (2007).

Williams discloses a long acting injectable formulation that includes a therapeutic agent, hydrogenated castor oil, and a hydrophobic carrier (*See*, Williams, column 3, lines 46-59).

Williams does not disclose each and every feature of the invention recited in independent claims 1 and 44. Specifically, Williams does not disclose or suggest a salt formed of the pharmacologically active compound and a *lipophilic counterion*. The Examiner asserts that the abstract discloses a formulation that includes capric acid. The abstract, however, does *not* disclose a formulation that includes capric acid. Rather, the abstract discloses “propyl dicaprylates/dicaprates, caprylic/capric acid triglycerides,” which are *esters* of caprylic acid and capric acid. Being *esters* of caprylic acid and capric acid, rather than the free acid, they are not capable of forming a salt with a pharmacologically active compound and, thus, are not a lipophilic counterion.

The Examiner states in the Office Action that

applicant asserts that the capric acid disclosed is capric acid triglyceride, which are esters of caprylic acid and capric acid, not capable of forming a salt with a pharmacologically active compound. However, **there is nothing in the claim that limits the lipophilic counterion to form a salt with the pharmacologically active compound.** The claim recites a composition comprising a salt of the pharmacologically active compound with a water miscible solvent. The lipophilic counterion can be an ionized form of a C<sub>1</sub>-C<sub>22</sub> saturated or unsaturated fatty acid.

(See, Office Action, pages 10-11, emphasis added). The Examiner also states in the Advisory Action that

the claim is drawn to a composition comprising a salt of the pharmacologically active compound “with” a lipophilic counterion and a pharmaceutically acceptable water immiscible solvent. The claim does not recite that the salt must form between the pharmacologically active compound and the lipophilic counterion and then combine the “resulting salt with a water immiscible solvent.”

(See, Advisory Action).

As discussed during the interview, the claims are directed to a salt that includes both the pharmacologically active compound and the lipophilic counterion. Applicants agree with the Examiner that “[t]he lipophilic counterion can be an ionized form of a C<sub>1</sub>-C<sub>22</sub> saturated or unsaturated fatty acid.” This is exactly the reason why Williams does not render the claims obvious. The lipophilic counterion must be charged, for example, by donating a proton. The specification clearly states

By a “lipophilic counterion” is meant an ionized form of a fat soluble molecule. The lipophilic counterion may be an ionized form of a fatty acid, but may also be another fat soluble molecule. The counterion has at least one charge opposite to that of a chemical group on an opposing salt member, thereby causing an ionic attraction between the two molecules.

(See, specification, ¶ [0013]). Williams, by disclosing *esters* of caprylic acid and capric acid, discloses compounds that cannot donate a proton. Therefore, the compounds disclosed in Williams *cannot* form a charged species that is required to form a salt (See, specification, ¶ [0012]). Being *esters* of caprylic acid and capric acid, rather than the free acid, the compounds disclosed in Williams are not capable of forming a salt with a pharmacologically active compound and, thus, are not a lipophilic counterion. Accordingly, there is no disclosure or suggestion in Williams of a salt formed between a pharmacologically active compound and a

lipophilic counterion, much less to combine this salt with a water immiscible solvent.

Moreover, there is nothing in Williams that would motivate one of ordinary skill in the art to form a salt between a pharmacologically active compound and a lipophilic counterion and to then combine the resulting salt with a water immiscible solvent.

In order to more clearly recite this feature, *i.e.*, that the claims are directed to a salt that includes both the pharmacologically active compound and the lipophilic counterion, independent claims 1 and 44 were amended, as agreed to during the interview, to replace the phrase “a salt of the pharmacologically active compound with a lipophilic counterion” with the phrase --a salt formed of the pharmacologically active compound and a lipophilic counterion--. Thus, the claims, as amended, address the Examiner’s concern that “there is nothing in the claim that limits the lipophilic counterion to form a salt with the pharmacologically active compound.”

For the reasons set forth above, Applicants respectfully request that the rejection of claims 1-5, 11, 12, 44, 45-48, 50, 51, 54, 55, 58-61, 67, and 68 under 35 U.S.C. § 103(a) as being obvious over Williams be reconsidered and withdrawn.

**The Rejection of Claims 1-8,11,12, 14, 44-51, 54, 55, 57-64, 67, 68, and 70 Under 35 U.S.C. § 103(a) as Being Obvious Over U.S. Patent No. 6,309,663 to Patel *et al.***

Claims 1-5, 11, 12, 44, 45-48, 50, 51, 54, 55, 58-61, 67, and 68 were rejected under 35 U.S.C. § 103(a) as being obvious over U.S. patent no. 6,309,663 (“Patel”) for the reasons set forth on pages 5-6 of the Office Action. Specifically, the Examiner asserts that Patel discloses a pharmaceutical composition for oral or parenteral use comprising an active agent, such as gentamycin or fluoxetine, that is combined with a hydrophobic surfactant (water immiscible solvent), such as castor oil, palm kernel oil, and corn oil, and ionizable surfactants that are in their ionized form, such as oleic acid, capric acid, linoleic acid, and lauric acid. Applicants respectfully traverse.

Patel discloses a triglyceride free pharmaceutical system having a dosage form of an absorption enhancing composition comprising at least two surfactants, at least one of which is hydrophilic, and a hydrophobic therapeutic agent (*See*, Patel, column 4, lines 1-5).

Similar to Williams, Patel does not disclose each and every feature of the invention

recited in independent claims 1 and 44, as amended, suggest the invention, or provide a reasonable expectation of success. Patel discloses an absorption enhancing formulation. Patel, however, does not disclose or suggest forming a salt between a pharmacologically active compound and a lipophilic counterion or to combine the resulting salt with a water immiscible solvent. The Examiner asserts that Patel discloses gentamycin and fluoxetine as a pharmacologically active compound. Each of these compounds, however, is simply included as part of a long laundry list of active compounds (*Id.* at column 29, line 41 to column 32, line 18). Similarly, the Examiner asserts that Patel discloses ionizable surfactants that are in their ionized form, such as oleic acid, capric acid, linoleic acid, and lauric acid. Again, the disclosure of these surfactants is part of a long laundry list of surfactants spanning over 10 pages of the patent (*Id.* at column 6, line 55 to column 29 line 5). There is, however, no disclosure or suggestion in Patel that would motivate one of ordinary skill in the art to select, from the long laundry list of active compounds recited therein, a pharmacologically active compound that can form a salt with a lipophilic counterion or to select, from the long laundry list of surfactants disclosed therein, a surfactant that is a lipophilic counterion, to then form a salt between the pharmacologically active compound and the lipophilic counterion, and then combine the resulting salt with a water immiscible solvent. Moreover, Patel provides no reasonable expectation that such a composition would successfully release the active compound over time.

In response to the argument that surfactants are part of a laundry list of active compounds, the Examiner states in the Office Action that

when the species is clearly named, the species claim is anticipated no matter how many other species are additionally named. *Ex Parte A*, 17 USPQ 2d 1716 (Bd. Pat. App. & Int. 1990) (The claimed compounds was named in a reference which also disclosed 45 other compounds. The Board held that the comprehensiveness of the listing did not negate the fact the compound claimed was specifically taught.

\* \* \*

In the instant case, the species is hydrophilic agents in which simple dissolution is not sufficient to provide efficient absorption of the therapeutic agent.

(*See*, Office Action, pages 11-12). The above matter is completely different from that in *Ex Parte A*. In *Ex Parte A* Applicant was trying to claim a single compound that was named within a list of compounds in the prior art. Applicants claimed compositions do not involve simply

claiming a composition that is recited in a list. Rather, Applicants discovery is a composition made by forming a salt of a pharmaceutically active compound and a lipophilic counterion and combining the salt with a pharmaceutically acceptable water immiscible solvent to form an injectable composition that releases the active compound over time when administered to an animal (claim 1) or is a clear solution (claim 44). Unlike the matter in *Ex Parte A*, Applicants composition is not a species that has been selected from a list of species in Patel. Patel does not disclose, much less even suggest, the composition claimed in independent claims 1 and 44. Patel merely discloses that using surfactants can enhance absorption of hydrophilic therapeutic agents using various absorption-enhancing components (*See*, Patel, column 3, line 51-53 and column 4, line 46-60). The present matter is clearly distinguished from that in *Ex Parte A*.

Applicant again notes that the Examiner states that “it is noted that the features upon which applicant relies (*i.e.*, forming a salt between a pharmacologically active compound and a lipophilic counterion) are not recited in the claims(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims” (*See*, Office Action, page 11). As agreed to during the interview and discussed above, the amendments to independent claims 1 and 44 address the issue that the salt is a salt formed between a pharmacologically active compound and a lipophilic counterion.

Moreover, and importantly, Patel, by disclosing a “an absorption enhancing composition” (*See*, Patel, column 4, lines 1-5 and column 45, lines 51-58) *teaches away* from the invention claimed in independent claim 1 that recites a “composition that releases the active compound over time when administered to the mammal.” Indeed, during the interview, the Examiner agreed that the disclosure of Patel is directed to compositions that are “absorption enhancing,” which is contrary to the recited feature of releasing “the active compound over time.” Patel, by teaching away from a feature required in independent claim 1, clearly cannot render independent claim and claims dependent therefrom obvious.

Applicants respectfully submit that the Examiner’s rejection of the claims is the impermissible use of hindsight in an attempt to reconstruct Applicants’ invention. The Examiner has used Applicants’ invention as a blueprint to combine selected parts of Patel, when there is no motivation to do so, to arrive at Applicants’ invention. It is well settled that hindsight cannot be

used to reject a claim as obvious. *In re Sernaker*, 702 F.2d 989, 994 (Fed. Cir. 1983); *In re Rinehart*, 531 F.2d 1048 (CCPA 1976); *In re Imperato*, 486 F.2d 585 (CCPA 1973); *In re Adams*, 356 F.2d 998 (CCPA 1966); *In re Anita Dembiczak*, 75 F.3d 994, 999 (Fed. Cir. 1999); *C.R. Bard Inc. v. M3 Systems, Inc.*, 157 F.3d 1340, 1352 (Fed. Cir. 1998) citing *Fromson v. Advance Offset Plate, Inc.*, 755 F.2d 1549, 1556 (Fed. Cir. 1985) (holding the prior art must suggest to one of ordinary skill in the art the desirability of the claimed combination). The Examiner is selectively picking and choosing various parts of the broad disclosure of Patel, absent a motivation to do so, to reconstruct Applicants' invention. Such hindsight reconstruction is impermissible as a matter of law.

The Examiner, however, states

it is not clear what picking and choosing is needed in order to determine what medicaments are specifically described in Patel et al. to determine which agents are included as part of the invention. *All that is needed to implement the disclosure of Patel et al.* is to combine any of the agents recited [ ] with the water immiscible solvents recited along with decanoic acid. There does not appear to be any difficulty in arriving at the decision.

(See, Office Action, page 12, emphasis added). The issue is not what “*is needed to implement the disclosure of Patel et al.*” The issue is what is need to implement the *claimed invention* in view of Patel. As discussed above, to arrive at Applicants' invention, one must first select a pharmacologically active compound that can form a salt with a lipophilic counterion from the long laundry list of active compounds recited in Patel (many of which do not form a salt), must then select a surfactant that is a lipophilic counterion from the long list of surfactants disclosed in Patel (many of which are not lipophilic salts), must then form a salt between the pharmacologically active compound and the lipophilic counterion, and then combine the resulting salt with a water immiscible solvent. Again, Patel is a vast disclosure and there is no motivation or suggestion to select the combination of components required to arrive at Applicants invention. Furthermore, as discussed above, there is no reasonable expectation that such a combination would provide a composition that releases the active compound “over time” because Patel teaches the opposite, *i.e.*, “an absorption enhancing composition.” The Examiner has used Applicants specification as a road map to pick and choose selected disclosures in Patel to arrive at Applicants invention without any motivation to do so and, in fact, with a teaching away from Applicants' invention.



For the reasons set forth above, Applicants respectfully request that the rejection of claims 1-8, 11, 12, 14, 44-51, 54, 55, 57-64, 67, 68, and 70 under 35 U.S.C. § 103(a) as being obvious over Patel be reconsidered and withdrawn.

#### **DOUBLE PATENTING**

Claims 1-14 and 44-70 were provisionally rejected on the grounds of non-statutory obviousness-type double patenting as being unpatentable over claims 65-138 of co-pending application serial no. 11/088,922 (“the ‘992 application”) for the reasons set forth on pages 6-8 of the Office Action. Specifically, the Examiner alleges that claims of the present application are not patentably distinct from the claims of the ‘992 application because the instant and conflicting claims recite substantially the same subject matter differing only in the description of the particular components claimed.

Applicants note that the rejection is provisional. Accordingly, once all rejections of the claims over prior art have been addressed, Applicants will submit a Terminal Disclaimer disclaiming the term of any patent that should issue from the above-identified application that would extend beyond the term of the ‘992 application.

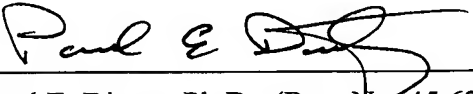
#### **CONCLUSIONS**

It is respectfully submitted that all claims are now in condition for allowance, early notice of which would be appreciated. Should the Examiner disagree, Applicants respectfully request a telephonic or in-person interview with the undersigned attorney to discuss any remaining issues and to expedite eventual allowance of the claims.

No fee is believed to be due for this submission. Should any additional fees be required, please charge the required fees to Kenyon & Kenyon deposit account no. 11-0600.

Respectfully submitted,

Date: April 4, 2008

  
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